REMARKS

Claims 1-20 are pending in the application. Claims 5 has been amended to incorporate claim 10. Claim 10 has been canceled. No new matter has been added by way of amendment.

I. Claim Rejections – 35 USC § 112

The Examiner rejects claims 5, 6 and 10-12 under 35 U.S.C. 112 as failing to comply with the enablement requirement. This rejection is traversed for the reason given below.

The Examiner objects to the above-referenced claims for a variety of reasons. Without acquiescing to the Examiner's arguments, the Applicant has amended claim 5 in the interest of furthering prosecution of this application. The Applicant reserves the right to pursue the subject matter encompassed by the original claim set in this or future applications.

In the Office Action, the Examiner objects that claim 5 recites a method of identifying cancer by obtaining a sample from any cell or tissue and assaying any gene set because while the specification is enabled for human H23 adenocarcinoma cells, the specification is allegedly not enabling for "any" cells. Claim 5 has been amended to specify a human patient and "a cell or tissue sample of cells or tissue suspected of comprising the lung adenocarcinoma." Claim 5 has also been amended to include the gene set from claim 10. The specification contains a detailed example identifying the recited gene set in human H23 adenocarcinoma cells. For lung adenocarcinomas, the specification clearly enables the use of at least a 40-gene set which is now recited in claim 5. Thus, these combined amendments clearly enable one of ordinary skill in the art to make and use the inventions recited in the claims. For at least these reasons, the claims at issue are enabled and withdrawal of the rejection is respectfully requested.

On page 5 of the Office Action, the Examiner appears to object that the specification is non-enabling for non-cancerous cells:

> ...although Applicants have identified at least 40 genes whose expression is down regulated at least 2 fold in cancer cells that overexpress exogenous RB2/p130, there is no indication that a non-cancerous cell that overexpresses RB2/p130 would give the same results.

35 U.S.C. 112 requires only that one skilled in the art be enabled to make and use the invention, and regulating genes in non-cancerous cells is not part of this invention. Thus, the Examiner's rejection is moot.

Assuming, *arguendo*, that the Examiner's rejection was pertinent, it would not require undue experimentation to test whether the same gene set would be down regulated in non-cancerous cells. Firstly, certain of the genes listed in amended claim 5 are known to be over-expressed in many types of lung cancers and not in non-cancerous cells, for example B-Myb, GRP-R, KPNA2, MKK3, PIM1, PLK1 and RAF-1. *See*, Provisional Patent Application 60/507,677, pages 7-9. Even if certain genes were not known to be over-expressed in non-cancerous cells, it would not require undue experimentation to test for down-regulation of a specific set of genes in healthy lung tissue. In re Wands provided the guidelines for determining undue experimentation:

(A) The breadth of the claims;
(B) The nature of the invention;
(C) The state of the prior art;
(D) The level of one of ordinary skill;
(E) The level of predictability in the art;
(F) The amount of direction provided by the inventor;
(G) The existence of working examples; and
(H) The quantity of experimentation needed to make or use the invention based on the content of the disclosure.

In re Wands, 858 F.2d 731, 737 (Fed. Cir. 1988). In Wands, the Court held that the specification was enabling with respect to the claims at issue and found that "there was considerable direction and guidance" in the specification, there was "a high level of skill in the art at the time the application was filed," and "all of the methods needed to practice the invention were well known." 858 F.2d at 740. After considering all the factors related to the enablement issue, the court concluded that "it would not require undue experimentation to obtain antibodies needed to practice the claimed invention." Id.

The case at hand is similar to the seminal case of Wands. First, there was a high level of skill in the art at the time the application was filed, which has been conceded by the Examiner. Second, all of the methods needed to practice the invention are well known. The specification describes fundamental laboratory techniques well known in the art for carrying out the invention. Finally, the specification provides explicit guidance on the type of tissue to be tested (non-cancerous lung tissue) and the specific genes to be tested. The test for undue experimentation is not merely quantitative, since a considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed. In re Wands, 858 F.2d

731, 737 (Fed. Cir. 1988). In this case, the only experimentation required is to follow the explicit guidance in the specification and to test for down regulation of a specific set of genes in a specific tissue. Such experimentation is clearly routine, and there is ample guidance in the specification to allow one of ordinary skill in the art to carry out the invention. This merely routine experimentation, even if considerable in amount, would not be undue as even a considerable amount of routine experimentation is permissible.

The Examiner alleges that "it is unpredictable that the results found in H23 lung cancer cells would also be found in non-cancerous cells, or in other cell types." Predictability, however, is not the test of undue experimentation. While the results of testing non-cancerous cells may or not be predictable, the results can certainly be obtained without undue experimentation.

Finally, the Examiner objects that "there is nothing in the specification (or found in the prior art) which demonstrates the level of down regulation that is sufficient to reliably predict the presence of cancer." The Examiner's objection, however, is based on an incorrect understanding of the principle of the invention. The down regulation of at least 2 fold alone does not predict the presence of cancer, but rather requiring a down regulation of at least 2 fold is necessary to ensure that a gene was in fact down regulated. A down regulation of more than 2 fold ensures that the measurement is accurate beyond errors in preparation and measurement of the sample. Only when down regulation of the specified gene set in the specified cell or tissue sample does the complete invention indicate the presence of cancer.

When viewed in that light, and contrary to the Examiner's assertion, there is ample evidence in the prior art that a cutoff ratio of at least 2 is appropriate and commonly used in previously developed microarray data analyses. The use of a cutoff ratio of at least 2 was a commonly accepted technique to measure down regulation of a gene at the time of the filing of this application. *See*, Scott D. Kobayashi et al., Down-Regulation of Proinflammatory Capacity During Apoptosis in Human Polymorphonuclear Leukocytes, J. Immunology 3358, 3357-68 (2003) ("Briefly, genes were defined as differentially expressed if the average expression level changed at least 2-fold..."); *See also*, W. Patrick Wechter et al., Gene Expression in Developing Watermelon Fruit, 9 BMC Genomics 275 (2008); Elisabetta A. Renzoni et al., Gene Expression Profiling Reveals Novel TGFβ Targets in Adult Lung Fibroblasts, 5 Respiratory Research 24 (2004). As discussed above, the inventions recited in the claims as amended are fully enabled. Withdrawal of the rejections and allowance of the claims is respectfully requested.

CONCLUSION

Based upon the foregoing remarks, Applicant respectfully requests reconsideration of this restriction requirement and early allowance of the pending claims. Should the Examiner feel that a telephone conference with Applicant's attorney would expedite prosecution of the application; the Examiner is urged to contact the undersigned attorney.

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Respectfully Submitted,

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